Calcineurin/NFAT signaling is required for neuregulin-regulated Schwann cell differentiation.

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Public Summary:
This article describes how a signaling pathway (calcineurin-NFAT) regulate neural development.

Scientific Abstract:
Schwann cells develop from multipotent neural crest cells and form myelin sheaths around axons that allow rapid transmission of action potentials. Neuregulin signaling through the ErbB receptor regulates Schwann cell development; however, the downstream pathways are not fully defined. We find that mice lacking calcineurin B1 in the neural crest have defects in Schwann cell differentiation and myelination. Neuregulin addition to Schwann cell precursors initiates an increase in cytoplasmic Ca^{2+}, which activates calcineurin and the downstream transcription factors NFATc3 and c4. Purification of NFAT protein complexes shows that Sox10 is an NFAT nuclear partner and synergizes with NFATc4 to activate Krox20, which regulates genes necessary for myelination. Our studies demonstrate that calcineurin and NFAT are essential for neuregulin and ErbB signaling, neural crest diversification, and differentiation of Schwann cells.

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